THE NEUROLOGICAL FEATURES OF ADDISON'S ANEMIA

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A tentative diagnosis may be established solely on neurological evidence.
The optic and auditory nerves bear the brunt of the attack in this disease.
Tingling and numbness in the hands and feet are the commonest symptoms.
Degeneration occurs in the peripheral nerves and also in ganglia.
There is apparently an endocrine phase.
Early diagnosis is all-important.
Arsenic is the drug of choice.
Treatment should be early, energetic, and persistent.

The clinical approach to Addison's anemia concerns chiefly the internist, but it is also a disease of peculiar interest to the neurologist. Twelve per cent of Woltman's series of cases complained of nervous symptoms alone, and 1.4 per cent presented neurological signs antedating the anemia. A tentative diagnosis may be established solely on neurological evidence.

The frequency of nervous system involvement in this disease is variously estimated. Hamilton and Nixon state that it occurs in 75 to 80 per cent of all cases of Addison's anemia. In Mix's series, the incidence was 60 per cent. Bramwell's series of cases showed an incidence of approximately 3 per cent. It would appear that Bramwell was far astray in his deductions when we consider the modern knowledge of this disease. The discrepancies in statistics some years ago were, no doubt, due to the fact that many cases of Addison's anemia were diagnosed as tabes, subacute combined sclerosis, or other system degenerations of the spinal cord. I have recently observed twenty-one cases of Addison's anemia, and nervous system lesions were demonstrable in 87 per cent.

REVIEW OF THE LITERATURE

In 1855 Addison first described the disease and noted mental derangement in such cases. He also observed degeneration of the solar plexus. In 1872 Biermer described the disease, and mentioned weakness and vertigo as prominent symptoms. Lichtenstern, in 1884, reported the association of pernicious anemia with tabes. There is little doubt that he confused tabes with the combined sclerosis of Addison's anemia. Lichtheim, in 1887, distinguished the combined sclerosis of Addison's anemia as a specific entity. Since then our knowledge of the nervous system lesions in this disease has progressed continually. The most able expositions on the subject are those of Russell, Batten, and Collier (1900), Bramwell (1915), Woltman (1918 and 1919), and Lurie (1919).

MENTAL SYMPTOMS

No psychosis was encountered in my series. Mental depression, querulousness, and irritability were common. Somnolence is not uncommon, even in early cases. One of my patients complained of cloudiness of the brain, a feeling of inertia and inability to concentrate. After a remission, euphoria is often noted. Apathy, melancholia, vertigo, and tinnitus often come on as the anemia advances. Osler noted delusions. Gulland and Goodall observed maniacal attacks, hallucinations and delirium occurring as terminal conditions. Greene says any form of mental disturbance may occur during the course of the disease. No striking psychical abnormalities occurred in the majority of Cabot's series. Jones and Raphael call our attention to the occasional resemblance of arteriosclerotic insanity and the mental disturbance of pernicious anemia. Barrett noted a definite paranoid trend in six of his eleven cases; also auditory hallucinations and a tendency to confabulation. Mental deterioration, as a rule, is not marked, the personality being fairly well preserved. Lurie's opinion coincides with Barrett's. Both suggest classifying these cases with the paranoid psychoses.

PATHOLOGICAL CHANGES IN THE BRAIN

The most important changes are areas of degeneration in the medulla, focal degeneration in the white matter and diffuse degenerations in the association tracts and commisures. Woltman describes destroyed areas in the cortical pyramidal cells; also in the pons and internal capsule. These degenerated plaques were closely associated with arteries, and he believes lymphostasis an important factor in their production. He also believes that these destroyed areas bear little relation to well-marked psychoses, but do account for the milder symptoms, such as apathy, depression, and delirium. Lurie found miliary foci in the pons in all his autopsied cases, and diffuse pigmentation of the nerve cells in three out of four. French found capillary hemorrhages in the meninges; also scattered petechial hemorrhage in the cortex.

CRANIAL NERVE SYMPTOMS

The optic and auditory nerves bear the brunt of the attack in this disease. Retinal hemorrhages are common, but the optic discs usually escape. In the author's twenty-one cases, the optic discs were paler than normal in eight. Small retinal hemorrhages were present in five. The area surrounding the disc is often edematous and the vessels dilated. Six cases of my series had tinnitus. One patient developed a bilateral deafness. Parosmia and paraguesia are occasionally found. Paresthesias of the tongue are common, and the patients complain of them when taking highly seasoned foods.

SPINAL CORD CHANGES AND SYMPTOMS

Tingling and numbness in the hands and feet are the commonest symptoms. The former usually appear first, but the paresthesias in the feet predominate later. Girdle sensations, especially about the knee, are frequent. Migratory sharp pains are sometimes complained of; also hyperesthesia of the trunk. Burning sensations in the toes often interfere with sleep, and a sensation of coldness or deadness in the extremities is not uncommon. Disturbances of the gait and station and spasticity of the limbs are frequently observed. Astereognosis and inco-ordination are occasionally noted. A sensation of swaying was the prominent complaint of one patient.

Pathology of Spinal Cord Changes—The spinal cord changes in Addison's anemia have been long recognized and thoroughly studied. Woltman finds that the degeneration begins in small isolated patches

in the posterior columns, and extends to the lateral columns by secondary degeneration and coalescence. The posterior columns and the lateral pyramidal tracts are most frequently involved. The anterior columns may be affected. The degeneration apparently begins in the nerve fibers, and is most marked at the mid-dorsal level. The direct cerebellar tracts are rarely degenerated. Blood vessel changes are usually insignificant. The meninges are seldom affected in Addison's anemia, but an increased cell count in the spinal fluid is occasionally present. Mix reports one such case. He also observed that pernicious anemia and syphilis attack the spinal cord in much the same fashion. The nerve roots, grey matter, and Lissauer's zone are rarely affected. The degeneration is most marked above the mid-dorsal level, yet the most pronounced neurological signs occur well below this region.

A number of cases are reported in which neurological signs were absent during life, but extensive cord degeneration was found at autopsy. Conversely, some cases presented neurological signs during life, but little or no cord degeneration at necropsy. The latter type of case is probably due to neuritis or a meningo—radiculitis. Constant system degenerations are not present in every patient with Addison's anemia. Unlike tabes, it does not breed true. The cord sclerosis in this affection is not a true system disease, but a diffuse, degenerative process which may involve any cord system.

Three types of cord changes are noted: the tabetic, the ataxic paraplegic, and a combination of the tabetic and ataxic types. In the tabetic type, the knee and ankle jerks are usually weak or absent, and the Babinski sign absent. Muscular hypotomnia followed by flaccidity is the rule. "Silk glove and stocking" anesthesia is sometimes present. The sharp demarcation between anesthesia and normal sensation in these cases is of interest. As in tabes, a sensation as of walking on cotton is not uncommon. Vibration sense is usually lost very early, and this is followed by loss of the muscle and position senses. Testicular sensation may be diminished, and there is often a hypaesthesia of the urethral and rectal mucosa. Epicritic sensibility is not involved to a great extent except in the cases showing glove and stocking anesthesia, but the response to stimuli is often delayed and localization is poorly performed. Except in the late stages, when anemia is profound and cord changes advanced, we do not usually find disturbance of pain or thermal sensations. Dissociation of sensibility is rarely encountered. Co-ordination is usually well preserved in the arms. Astereognosis is common; also loss of manual dexterity. Rombergism is well marked in the late stages of the disease, but may be absent during the stage of irritation. The gait in far-advanced cases is distinctly tabetic.

The ataxic paraplegic type is characterized by spastic paralysis of the legs, exaggerated knee-jerks, patellar and ankle clonus, as a rule, and a bilateral Babinski. As the sensory tracts are intact, there are no sensory disturbances. This type is totally unlike the tabetic. The lateral pyramidal tracts bear the force of the attack; consequently, we get a syndrome resembling spastic spinal paraplegia. In the early stages one finds only spasticity and increased reflexes plus a positive Babinski.

In the combined type we find simply an addition of the spastic paraplegia symptoms to those of the tabetic type. In these cases Mix points out that the behavior of the reflexes is governed by the involvement of the pyramidal tracts; that is, the increased reflexes, Babinski sign, ankle clonus, and spasticity remain even when the posterior columns are extensively degenerated. This type is the subacute combined sclerosis, and is usually a late manifestation. The tabetic type is the most common, the subacute combined sclerosis next, and finally the ataxic paraplegic type.

PERIPHERAL NERVE SYMPTOMS

It is now firmly established that degeneration occurs in the peripheral nerves and also in ganglia. The peculiar sensory symptoms in Addison's anemia cannot be explained on the basis of cord involvement alone, but most observers believe that peripheral nerve degeneration is an inconstant finding. Nonne found no striking changes in the posterior roots or peripheral nerves. Putnam and Taylor found insignificant changes in the same areas. Bramwell believed absence of nerve degeneration to be characteristic of the disease. Von Noorden, however, found definite evidence of neuritis in his series, while Hamilton and Nixon noted distinct areas of degeneration in the posterior roots, Lissauer's zone, and the anterior tibial nerves in six out of ten necropsied cases. Woltman found objective evidence of multiple neuritis in 4 per cent of his cases. He thinks the sensory symptoms can be better explained on the basis of multiple neuritis than on that of spinal cord change. The "stocking and glove" anesthesia, in his opinion, is due to a neuritis. Temperature, touch, and pain sensibilities may be lost, but are usually almost intact.

ENDOCRINE GLAND DYSFUNCTION

There is apparently an endocrine phase to Addison's anemia. In a broad sense the blood-forming organs, spleen, lymphatic glands, and thymus are links in the endocrine chain, and we know that these organs and other ductless glands are affected in this type of anemia. It is certainly true that, in the type of pernicious anemia with excessive hemolysis, splenectomy brings about marked temporary improvement. In these cases we may assume that a hormone in the blood stimulates the excessive hemolysis, that splenectomy breaks this vicious cycle, and improvement results. Sailer pointed out that gonad dysfunction was occasionally seen in this disease. Draper also states that many cases of Addison's anemia have associated endocrine syndromes.

SPINAL CORD BLADDERS

Spinal cord bladders are common in advanced primary anemia. Kretschmer emphasized the fact that little attention has been paid to this condition, and that these patients often come first to the urologist. Difficult urination followed by partial retention, then incontinence, and finally complete retention is the usual sequence of symptoms. Six cases of my series were studied cystoscopically, and fine tra-

beculations in the bladder mucosa were found in four. This was very marked in two. The internal sphincter is often relaxed. Cystograms reveal a funnel-shaped bladder contrasting markedly with the spherical outline of the normal cystogram.

DIFFERENTIAL DIAGNOSIS

Tabes is most commonly confused with Addison's anemia. Optic atrophy and the Argyll Robertson pupil spell tabes. They are unknown in Addison's anemia. Knee-kicks are diminished or absent in tabes, whereas in Addison's anemia they are often increased, due to combined sclerosis. Sanford shows that a Babinski sign is often present in Addison's anemia, but is never present in tabes. Retinal hemorrhages are present in 50 per cent of cases of primary anemia. The Wassermann reaction and blood studies will differentiate the two conditions in most cases. Lastly, Addison's anemia associated with late or latent syphilis is quite rare.

Disseminated sclerosis may be distinguished from primary anemia by the following points: 1. It rarely occurs after 35 years, whereas pernicious anemia is rare before this age. 2. It is more common in females, whereas pernicious anemia is twice as common in males. 3. It is very chronic, whereas Addison's anemia usually kills within three years. 4. It is not associated with anemia. 5. Nystagmus, intention tremor, staccato speech, optic atrophy, and transitory monoplegias are uncommon in Addison's anemia.

Combined scleroses due to secondary anemia, pellagra, plumbism, leukemia, and syphilis may usually be differentiated by careful studies of the blood, nervous system, and gastric contents.

TREATMENT

Early diagnosis is all-important. Careful neurological examination will often help to establish diagnosis before anemia appears. Focal infections should be eradicated, and the results are often good.

Diluted hydrochloric acid given either before or after meals is of distinct value. The iron preparations are of no value. Arsenic is the drug of choice. Fowler's solution, in ascending dosage, is beneficial, but should be discontinued for one week in every four to avoid arsenical neuritis. Salol is often useful to check diarrhea and intestinal putrefaction. Constipation must be corrected and intestinal parasites eradicated. Rest, sunshine, and fresh air are most important, and rest in bed is obligatory if the erythrocytes are less than 2,000,000.

Neosalvarsan or silver salvarsan are most useful. If the erythrocytes are above 2,000,000, they may be given once a week until improvement occurs, then less often. Three-tenths gm. of neosalvarsan or one-tenth gm. of silver salvarsan are given at first, and the dosage gradually increased.

Blood transfusion is unnecessary if the erythrocytes are over 2,000,000. In cases with excessive hemolysis, it is useful. The citrate method is the simplest. Five hundred cc. of blood is given every fourth day until improvement begins, then neosalvarsan is resumed. Reactions occur more commonly after using citrated blood, but this is overcome by morphine and atropine in full dosage before beginning the transfusion.

Splenectomy is not routinely advisable. Splenectomy gave marked temporary improvement in two of my patients with excessive hemolysis and splenomegaly.

Tonics are harmless and sometimes do good.

A diet rich in vitamins and containing a moderate amount of protein is advised. It is difficult to control the distressing paraesthesias and nervous manifestations. Neosalvarsan has a beneficial effect on them at times. Temporary relief is obtainable by using antispasmodics.

Irradiation of the spleen and long bones has been of no value in my cases.

I have had no experience with germanium dioxid. Shukle and Muller and Izard report on it favorably.

Psychotherapy is often useful.

We should not give a gloomy prognosis in these cases, but treat them early, energetically, and persistently. In this way the patient's life is prolonged, and we may even prevent the appearance of the full-blown disease.

CONCLUSIONS

1. Nervous system involvement occurs in 80 per cent or more of patients with Addison's anemia.
2. Degenerative changes in the brain and mental symptoms are quite common.
3. The cranial nerves, with the exception of the optic and auditory, usually escape damage.
4. Spinal cord degeneration occurs in 80 to 87 per cent of cases.
5. Sensory symptoms, especially the various paraesthesias, are the commonest neurological findings.
6. Deep sensation is impaired earlier and to a greater extent than superficial.
7. Three main types of cord change occur: (1) The tabetic; (2) subacute combined sclerosis; and (3) the ataxic paraplegic.
8. Peripheral nerve degeneration is commoner than is generally believed.
9. Endocrine dysfunction is a common complication.
10. Spinal cord bladders may be recognized early by the urologist.
11. Tabes dorsalis is the disease most commonly confused with Addison's anemia.
12. Early diagnosis is essential if good results are to be obtained by treatment.
13. Careful neurological examination may establish a presumptive diagnosis before the anemia develops.
14. Treatment should be early, energetic, and persistent.

Farmers and Merchants' Bank Building.

DISCUSSION

Charles E. Nixon, M. D. (Flood Building, San Francisco) — Since Lichtenstern and Lichtheim noted changes in the spinal cord in cases of pernicious anemia many observers have offered their explanation of the mechanism by which these lesions are produced. While the majority of neuropathologists believe that the lesions of the nervous system are caused by a toxin, they are not agreed as to the way in which the toxin acts. Seyderhelm has recently made an interesting contribution to this phase of the subject. He

was able to break up the toxin "Oestrin" into various fractions. The toxin was both hemolytic and neurotoxic; he found that the "blood poison" acts ("both as a hemolytic and toxic agent") only by parenteral introduction.

Several types of lesions are found in the spinal cords of these cases, but the most characteristic change consists of a degeneration of the long fibers of the cord, particularly of those in the posterior column. It is fairly well established that the long uncrossed fibers of the posterior column conduct impulses having to do with vibratory sense, and this explains the fact noted by Dr. Cole that vibration sense is usually lost very early.

The peripheral nerve involvement which has been demonstrated pathologically is responsible for the acroparesthesiae so prominent in most cases of subacute combined degeneration of the cord associated with pernicious anemia. The patients complain of "tingling," "prickling," "numbness" (using this word at times to express paresthesiae and at other times to denote loss of tactile sensibility), "a feeling like sand on the finger tips that can't be picked off."

The combination of subjective sensory disturbances and loss of vibration sense is the most characteristic picture in this condition.

Ross Moore (520 West Seventh street, Los Angeles)—This very meaty paper of Dr. Cole's would be hard to discuss were one to consider it paragraph by paragraph. His series of twenty-one cases of Addison's anemia is rather an extensive one and his analysis is first class.

The chief value of this paper to my mind lies in its suggestiveness. To everyone who reads it carefully it brings a sense of the fact that nervous disorders are frequently part and parcel of more general system conditions. We have really known this a long time, but we do not always keep it in mind. The last fifty years of medicine has seen a great taking to pieces of disease and a great cataloging of symptoms. We are now on the opposite tack—we are synthesizing disease on the basis of fundamental biological principles. Thus it comes about that we hitch Addison's anemia and such a clinical picture as tabes dorsalis together at times. Hitching them together provides a new concept of the individual case and points the way to a rational program of treatment.

Thus medicine advances.

Fred B. Clarke, M. D. (Pacific-Southwest Building, Long Beach, Calif.)—We are all indebted to Doctor Cole for a most excellent review of the literature pertaining to the pathology and symptomatology of Addison's anemia as related to the nervous system. It is possible to make a diagnosis of pernicious anemia from the symptoms of spinal cord involvement before the charactertistic blood changes are found. In many instances they antedate blood changes from two to three years. Bramwell has reported a case in which the time was three years.

Doubtless many cases diagnosed as sub-acute, combined degeneration of the cord, in which a typical blood picture is not found, would have shown the true nature of the anemia at autopsy. Why the clinical picture should be so varied as to lead, in some cases, to a diagnosis of Addison's anemia with spinal cord changes of sub-acute combined degeneration, and in others to sub-acute combined degeneration with anemia, is hard to understand, unless one believes that in some cases the toxins may have a more marked hemolytic action, and in others a more marked neurotoxic action. Some authorities believe that two separate and distinct toxins are to be considered, one showing a predilection for red blood cells and the other for the nervous system.

Regardless of whether the anemia occurs before changes in the nervous system are manifest or afterward, there is no difference in the neurological symptoms nor in the pathological changes in the cord, except in degree.

I think it is well to emphasize that tingling and numbness of the fingers or toes are very valuable as early symptoms and when persistent should result in a careful search for confirmatory evidence of anemia.

The disturbance of vibratory sense I regard as of great importance, occurring as it does so frequently and constantly in the majority of cases before a diagnosis can be made from the blood findings. The same is true of joint sense, both being conducted by the same pathway.

The mental symptoms are interesting and occur more often than usually recognized. Barrett in 650 necropsies on insane persons in Michigan found fifteen to have brain changes of pernicious anemia.

Doctor Cole has said in his conclusions that early diagnosis is essential, with which I most heartily agree, and I believe we should, in so-called mild anemias of unknown cause, critically analyze any disturbance of the digestive tract, especially with reference to achlorhydria, as this is undoubtedly the earliest and most reliable finding in pernicious anemia. Many well authenticated cases have shown this symptom as early as twelve years before blood and cord findings became present. Achlorhydria, if carcinoma of the stomach is not present, should be looked upon with grave suspicion that the individual presenting such a finding either has or may become a sufferer of Addison's anemia.

V. R. Mason (Pacific Mutual Building, Los Angeles)—This presentation of the neurological features of pernicious anemia is so complete that little is left for discussion. It is of interest that in Cabot's large series changes in the nervous system were present in 87 per cent of autopsies in this disease. Dr. Cole has shown that symptoms referable to the nervous system are present in only a slightly lower percentage. It is, therefore, important that internist and neurologist work together in an effort to arrive at an early diagnosis.

Sub-acute degeneration of the cord is usually due to pernicious anemia, and in the vast majority of such cases the clinical picture is due to implication of the long fibers of the posterior columns, a fact emphasized by Dejerine. Such neurological findings often precede the development of anemia, but in my experience they very rarely precede the qualitative alteration of the blood on which a presumptive diagnosis may be made.

I should also like to emphasize two other points of some importance. In the first place, improvement of the neurological symptoms rarely occurs; and secondly, in certain instances, the progress of the degeneration of the nervous system may occur with great rapidity.

Walter C. Smallwood, M. D. (701 Pacific Avenue, Long Beach, Calif.)—Doctor Cole has very completely presented the neurological features of pernicious anemia and has placed due emphasis upon the great frequency of nerve involvement in this disease.

Brain, cord, or peripheral nerve elements may be affected, but cord symptoms are the most common and peripheral lesions most rare.

There is no typical picture of cord involvement in Addison's anemia, but the dorsal and lateral columns are most usually affected, either singly or in combination. The degree of involvement is remarkably variable, and the predominance of impairment may be exhibited in either column, or both columns may be more or less equally affected.

Symptomatically, paresthesias of the feet and hands are the earliest and most common manifestations. Tabetic types of cord implication with inco-ordination and loss of reflexes occur more frequently than spastic or spastic-ataxic syndromes. Occasionally more complex and bizarre neurological findings point to a cord degeneration of a very diffuse and patchy nature.

Disturbances of the nerve function may antedate the anemia, although qualitative alterations in the blood smear have always been present in my experience.

Symptoms of peripheral nerve involvement are rare; stocking and glove anesthesias I have not seen.

Bladder involvement is frequent; fecal incontinence is rare.

Objective neurological evidence may be but slightly marked in pernicious anemia, but if carefully sought is exceedingly common. Hypesthesia or hypalgesia, especially in the legs, diminution or loss of vibratory sense, and slight inco-ordination in the legs possibly visible only in the excessive play of the dorsal tendons in the Romberg test, may be the only signs of damage to the spinal cord.

Neurological findings are more constant and more pronounced as the age scale is advanced. Reviewing our own series, the nervous system showed implication in 95 per cent of patients who had passed the fifth decade.

The neurological symptoms due to cerebral involvement are manifested more by psychic disturbances than by physical nervous stigmata. Pathologically, however, diffuse degenerative plaques in the white matter of the brain are frequently found.

The cranial nerves are almost constantly spared.

Marked mental disturbance, hallucinations, delirium, and maniacal states are ordinarily terminal events. Less profound changes, apathy, somnolence, and mild confusion are not infrequent, especially in the blood crises, and remissions are often attended with improvement or complete amelioration.

Treatment of any type has been, in my own experience, of little avail when definite organic neurologic lesions could be demonstrated.

Doctor Cole (closing)—I have very little to add to the excellent discussion on this paper. Dr. Clarke has emphasized two very important diagnostic points, namely, the early achlorhydria in these cases, and the paraesthesias in the fingers and toes. As he points out, when we are confronted with a patient who has an obscure digestive disorder and in whom we find an achlorhydria, we should immediately think of pernicious anemia and look for other objective findings in the blood smear and the nervous system.

I wish to thank Dr. Moore for again reminding us all that nervous system disorders are often the expression of some underlying systemic condition. We forget this fact much too often.

I cannot fully agree with Dr. Mason that improvement in the neurological symptoms rarely occurs. In my experience I have found that, as a rule, improvement in the blood picture is usually coincident with improvement in the subjective nervous symptoms.

Dr. Nixon lays special stress on the pathology of the nervous system degenerations in this disease, and rightly so, for I know of no disease apart from syphilis which gives rise to so many striking pathological alterations in the nervous system.

Dr. Smallwood points out that the neurological findings are more constant and pronounced as the age scale advances. I omitted mention of this in my paper.

The whole subject is a very fascinating one. The research worker who discovers the real cause of pernicious anemia and devises a successful method of treatment or cure will have generations to come rising up to call him blessed.

(From the Department of Internal Medicine, Johnston-Wickett Clinic, Anaheim, California.)

You can't starve a cow and expect a record-breaking milk yield. Your estate cannot collect on your life insurance unless you pay the premiums. A slow, but sure, method of business suicide is the elimination of all promotion.—Facts Regarding Pharmaceutical Promotion.)—S. De Witt Clough.

"If the people do not generally approve a law, speeding up prosecutions will not make them love it. An increasing number of arrests does not prove that a law is operating successfully, but only that an increasing number of people are doing the things for which they may be arrested."

SKIN SYPHILIS AS CLINICAL ENTITY

By MOSES SCHOLTZ, M. D.,

(From the Graduate School of Medicine, University of California, Los Angeles County and Kaspare Cohn Hospitals)

The controversy over who should treat syphilis is not settled yet.

Diagnostic errors are mostly those of omission rather than of commission.

The Wassermann test does not deserve such absolute confidence.

A syphilitic lesion may be elevated above the skin, but it is never limited to the epidermis only.

Syphilitic lesions involute either by absorption or ulceration, with subsequent production of scars.

There is a great and lamentable tendency at present in the profession to lean too heavily on the laboratory in making a diagnosis.

Laboratory findings are valuable and acceptable in dermatology only in correlation and checked up by clinical evidence.

It is gratifying to a clinician to hear serologists calling halt on the overzealous believers in the Wassermann test and reminding them that laboratory findings should not be considered alone, but only in correlation with clinical findings.

If there is one disease that belongs at once to all medical specialties, this is syphilis. Syphilis is truly a bone of contention among various specialties. The controversy over who should treat syphilis is not settled yet.

A case of syphilis may or may not affect a certain organ or system of organs in the body, but every case of syphilis must go through cutaneous manifestations—at least, limited to the primary chancre. After the resolution, the active syphilides often leave permanent traces, such as scars, pigmentations, leucodermata, which are of considerable retrospective diagnostic importance. Hence, familiarity with skin syphilis as a whole is of great clinical value to the medical man, no matter in what special line he may be working.

I shall briefly review the most common clinical types of syphilides, their salient diagnostic features, and shall briefly consider the sources of most common diagnostic errors in syphilis.

DERMOTROPIC VS. NEUROTROPIC SYPHILIS

There is a current view that incidence of skin manifestations in syphilis depends on the strain of spirochetae. It is believed that various strains preferentially attack various organs of the body; hence, there are: Dermotropic strain, neurotropic strain, etc. There is also a belief that there is a kind of inverse relationship between the involvement of the skin and other tissues by spirochete; that is, the more profuse and marked the skin eruptions are the less likely is the involvement of visceral organs, and vice versa. However, this hypothesis is not sufficiently substantiated by clinical evidence.

GENERAL MORPHOLOGIC CHARACTERISTICS

Speaking of the general morphologic characteristics of cutaneous syphilis, one outstanding feature should be emphasized: the most incredible morphologic versatility and polymorphism of skin syphilis. It can truly be said that syphilis can mimic any dermatologic lesion whatever. So true it is that the